

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of the Claims:

1 - 45. (Canceled)

46. (New) A nucleic acid sequencing method comprising:

providing a DNA sample containing a plurality of circular single-stranded DNA template molecules each comprising a rolling circle amplification (RCA) primer-annealing sequence and a target sequence, each target sequence being a fragment from a shotgun library;

annealing an RCA amplification primer to said RCA primer-annealing sequence of the template molecules, and amplifying the target sequences by rolling-circle amplification, wherein the rolling circle amplification products are randomly immobilized on a solid support;

sequentially probing the solid support with a panel of probes, and preparing hybridization spectrums for the amplified target sequences;

identifying the location of the target sequences within a reference sequence by comparing the hybridization spectrums to expected hybridization spectrums for the reference sequence, with a highest scoring spectrum within the reference sequence representing the likely location of a target sequence; and

identifying any differences in sequence between the target sequences and the reference sequence by resolving discrepancies between the hybridization spectrums for the target and said highest scoring spectrum.

47. (New) The method of claim 46, wherein the differences in sequence are one or more of single nucleotide polymorphism, insertion, deletion, alternative splicing, an alternative transcriptional start site, alternative polyadenylation, and microsatellites.

48. (New) The method of claim 46, wherein the panel of probes comprises probes with specificity that is an effective specificity of 3 to 10 bases.

49. (New) The method of claim 48 wherein the effective specificity is 4 to 6 bases.

50. (New) The method of claim 46, wherein the size of each target sequence and the effective specificity of the probes are adjusted so that the statistical probability of hybridization of each probe to each target is between 25% and 75%.

51. (New) The method of claim 50, wherein said statistical probability is between 40% and 60%.

52. (New) The method of claim 46, wherein the reference sequence is from the same species as the target sequence.

53. (New) The method of claim 46, wherein the reference sequence is from a different species from the target sequence.

54. (New) The method of claim 46, wherein the rolling circle amplification products are immobilized on the solid support at random locations with a density of between 10^3 and 10^7 per cm^2 , and wherein the fragments from the shotgun library have approximately the same length.

55. (New) The method of claim 54, wherein each rolling circle amplification product comprises at least 1000 tandem-repeated copies of a target sequence.

56. (New) The method of claim 54, wherein said density is between 10^5 per cm^2 and 10^7 per cm^2 .

57. (New) The method of claim 54, wherein the target sequences have the same length within 10% CV.

58. (New) The method of claim 57, wherein the target sequences have the same length within 5% CV.

59. (New) The method of claim 54, wherein said shotgun library is an RNA library, an mRNA library, a cDNA library, a genomic DNA library, a plasmid DNA library or a library of DNA molecules.

60. (New) The method of claim 46, wherein, in the panel of probes:

each probe contains an oligonucleotide,

each said oligonucleotide is stabilized,

each said oligonucleotide carries a reporter moiety,

each probe has an effective specificity of between 3 and 10 bp, and

the panel of probes is such that at least 10% of all positions in an arbitrary target sequence statistically hybridize with at least one probe in the panel.

61. (New) The method of claim 60, stabilized by one or more of introduction of degenerate positions, introduction of locked nucleic acid monomers, introduction of peptide nucleic acid monomers, and introduction of a minor groove binder.

62. (New) The method of claim 60, wherein the reporter moiety is selected from the group consisting of a fluorophor, a quencher, a dark quencher, a redox label, and a chemically reactive group which can be labeled by enzymatic or chemical means.

63. (New) The method of claim 46, wherein the hybridization spectra are compared using a spectral search instrument comprising a field-programmable gate array (FPGA) attached to a host computer and a computer-readable memory device, wherein:

said FPGA is configured to perform spectral search,

said computer-readable memory device stores a reference nucleotide sequence and a set of hybridization spectra,

said host computer is configured to provide said FPGA with the reference nucleotide sequence and with each said hybridization spectrum,

said FPGA, when provided with a reference nucleotide sequence and a hybridization spectrum, writes to said computer-readable memory to store the location or locations of best matches between said hybridization spectrum and said reference nucleotide sequence.